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Diffuse Cystic Renal Dysplasia: Nonsyndromal Familial Case

Masakatsu Sase, Masato Tsukahara, Atsushi Oga, Noriko Kaneko, Masahiko Nakata, Tsuyoshi Saito, and Hiroshi Kato

Departments of Obstetrics and Gynecology (M.S., N.K., M.N., T.S., H.K.), and Pathology (A.O.), Yamaguchi University School of Medicine, School of Allied Health Sciences (M.T.), Yamaguchi University, Ube, Japan

We report on a family in which three individuals, a male and two females were affected with nonsyndromal diffuse cystic dysplasia of the kidneys. The parents had no renal abnormality. The occurrence of diffuse cystic dysplasia in three sibs born to normal parents suggests autosomal recessive inheritance. ©1996 Wiley-Liss, Inc.

KEYWORDS: familial occurrence, diffuse cystic renal dysplasia, autosomal recessive inheritance

INTRODUCTION

Cystic disorders of the kidney in the fetus and newborn can be divided into those of genetic origin and those of apparently non-genetic, developmental origin. Some of the latter previously thought to be developmental origin, are proving to be familial disorders. We report here on a family in which three sibs were affected with diffuse cystic renal dysplasia.

CLINICAL REPORTS

Case 1

The pedigree of the family is shown in Figure 1. A 24-year-old G2P0 woman (I-2) was referred because of oligohydramnios at 25 weeks of gestation. The course of pregnancy had been completely normal until oligohydramnios was noted at 25 weeks of gestation. Ultrasound examination showed that her fetus had two large abdominal masses and tricuspid regurgitation and cardiomegaly. The fetal bladder was not detected. Rupture of membranes occurred spontaneously at 28 weeks of gestation. The volume of amniotic fluid was scanty. The infant (II-2) weighed 1,120 g (−0.2 SD) but died soon after birth. There was no anomaly of external appearance. Chromosomes were normal (46,XY).

Autopsy showed severely hypoplastic lung; both kidneys had numerous cysts of various size, renal lobulation was indistinct, the pelves were patent, the calyces were not defined, and the medullary pyramids were absent (Fig. 2a). Thread-like ureters and the bladder were present on gross examination but the ureters were lost at dissection and fixing. Ebstein anomaly was recognized in his heart. No other malformations were found in other organs.

Microscopically, most of the renal cysts were lined by columnar or cuboidal epithelium and often surrounded by connective tissue without foci of cartilage. There were a few glomeruli and nephrogenic tissue was scattered among various sized cysts (Fig.3a).

Ultrasound examinations of the healthy mother and her non-consanguineous 30-year-old husband (I-1,2) showed no abnormalities of kidneys and urinary tracts. In the present family, there was no knowledge of any previous relative with renal disease of any type and no unexplained early death.

Case 2

At age 26 years the mother had a spontaneous abortion at 6 weeks of gestation. At 28 years she was referred at 19 weeks of gestation because of oligohydramnios. Transvaginal ultrasonographic examination showed many small cysts in the kidneys of the fetus. The renal pelves were visible as a lucent echo area in the kidneys. The fetal bladder could not be detected. At 21 weeks of gestation, she decided to terminate the pregnancy and delivered a female infant (II-4) with a birth weight of 360 g. The newborn infant had no anomalies of external appearance. Chromosomes were normal (46,XX).

Autopsy showed hypoplastic lungs and numerous, variable size renal cysts up to 1 cm. Macroscopically, her kidneys looked like the kidneys of case 1. The ureters were thin but patent, and the bladder was hypoplastic (Fig. 2b). No other malformations were found.

Microscopic findings were similar to the kidneys of case 1. However, the amount of connective tissue between cysts was larger and the kidneys were more immature (Fig. 3b).

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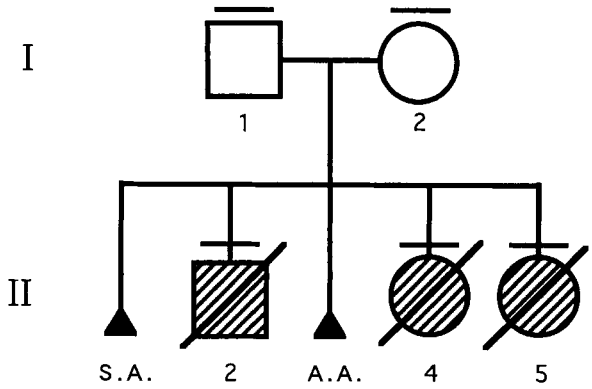
Address reprint request to Dr. Masakatsu Sase, Department of Obstetrics and Gynecology, Yamaguchi University School of Medicine, Ube, Yamaguchi, 755 Japan.



S.A. ; Spontaneous Abortion
A.A. ; Artificial Abortion

Fig. 1. Pedigree.

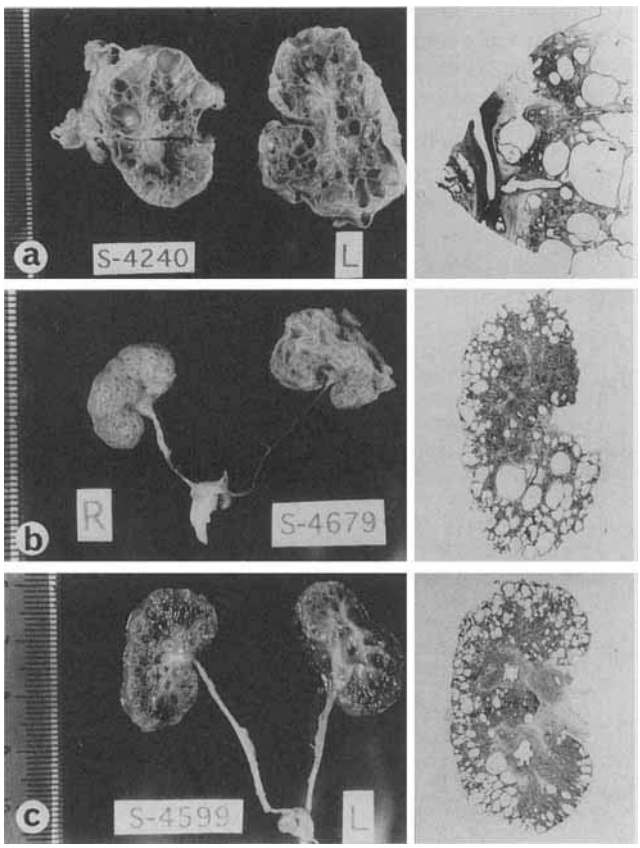


Fig. 2. Gross appearance (left part) and transverse section (right part) of the kidneys in three sibs. **a:** case 1. **b:** case 2. **c:** case 3.

Case 3

At age of 30 years, the mother was referred at 15 weeks of gestation for oligohydramnios. Transvaginal ultrasonographic examination showed many small cysts in the kidneys of the fetus and oligohydramnios.

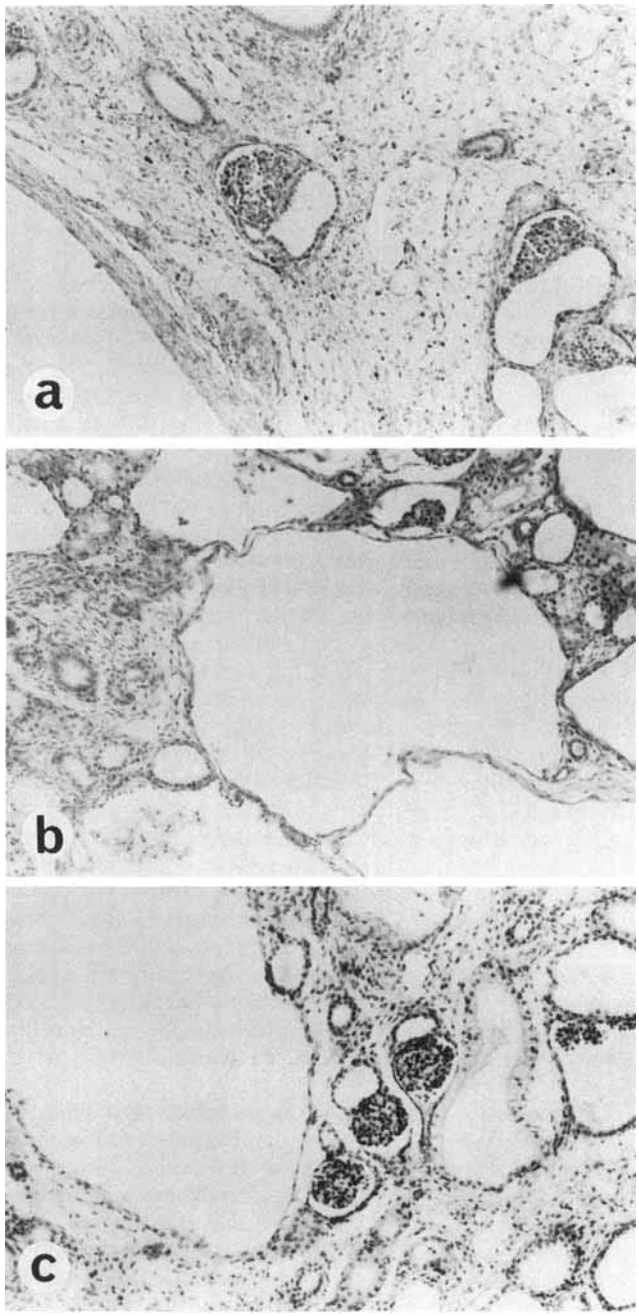


Fig. 3. Microscopic photograph of the kidney in three sibs. **a:** case 1. **b:** case 2. **c:** case 3.

The renal pelves and bladder were visible as a lucent echo area. Although serial measurements of the fetal bladder were performed for 2 hours with the maternal furosemide injection at 19 weeks of gestation, the fetal bladder did not enlarge during the observation period. She decided to terminate the pregnancy and delivered a female infant (II-5) with a birth weight of 250 g at 19 weeks of gestation. No anomaly was found on external appearance. Autopsy showed hypoplastic lungs and cystic kidneys. Macroscopic and microscopic findings were like those of case 2 (Figs. 2c, 3c).

Reexamination of the ultrasound findings in the parents showed no abnormalities.

DISCUSSION

The clinicopathologic manifestations of these three cases described here fit the criteria of diffuse cystic dysplasia of the kidney [Bernstein, 1992]. Expression of diffuse cystic dysplasia within this family was similar.

"Diffuse cystic dysplasia" refers to the occurrence of multiple, fairly regular, and mainly cortical cysts ranging from a few mm up to several cm in diameter in both kidneys. The medullary pyramids are poorly formed and contain scanty primitive ducts. Ductal and nephronic structures are generally scanty and metaplastic cartilage unusual. While there is a superficial resemblance to multicystic dysplasia, diffuse cystic dysplasia can be distinguished by the invariably bilateral renal involvement and the presence of some degree of renal pelvic development with a patent ureter. In diffuse cystic dysplasia, the gross cystic changes and bilateral involvement may suggest the possibility of autosomal recessive polycystic disease. However, diffuse cystic dysplasia lacks the characteristics of latter condition, such as the preserved reniform shape and corticomedullary demarcation of the kidneys and tendency of the kidneys to collapse on sectionings as fluid drains from the cut surface [Risdon, 1992].

Autosomal dominant polycystic disease (ADPKD) must also be considered in the differential diagnosis. Despite the genetic homogeneity the patterns of ADPKD are highly variable. There are no relatives of the parents with suffer renal failure. The repeated ultrasound examinations of the parents at age between 26 and 30 years did not show the expected abnormal appearance of the kidneys. Bear et al.[1992] reported that most ADPKD is diagnosed ultrasonographically by age 30 years. Liver cysts, which are seen in approximately 50% of ADPKD cases, and intracranial aneurysm, were not seen in our cases. Altogether, we think ADPKD is unlikely in our cases.

Diffuse cystic dysplasia is often seen in malformation syndromes such as Meckel syndrome, renal-hepatic-pancreatic dysplasia, Zellweger syndrome, Jeune syndrome, Majewski syndrome, Saldino-Noonan syndrome, Ellis-van Creveld syndrome, Elejalde syndrome, Robert syndrome, Smith-Lemli-Opitz syndrome, and VATER association or chromosomal abnormalities such as trisomy 9 and trisomy 13 [Bernstein, 1992]. However, the fact that three cases described here had no anomalies on appearance, and showed no malformations of internal organs (except case 1: Ebstein anomaly) excludes the other syndromes.

Diffuse cystic dysplasia occasionally occurs as an isolated anomaly, and it may be sporadic. The pedigree of this family suggests a genetic origin. The occurrence of isolated diffuse cystic dysplasia in three sibs of different sex, with normal parents, can be explained on basis of dominant inheritance with reduced penetrance, autosomal recessive inheritance, and multifactorial determination. An alternative explanation may be germinal mosaicism. Familial occurrence of the nonsyndromal condition is rare. To our knowledge, there is only one report regarding familial occurrence of diffuse cystic dysplasia. Cole et al.[1976] reported bilateral cystic renal dysplasia in three sibs (two females and one male) who were born to non-consanguineous parents with apparently normal kidneys. These cases fit the criteria of diffuse cystic dysplasia. He suggested that the occurrence of the dysplasia in three sibs would be compatible with autosomal recessive disease. We also think that autosomal recessive inheritance is a more reasonable explanation than dominant inheritance or multifactorial determination.

Diffuse cystic dysplasia may also be an occasional manifestation of hereditary renal adysplasia [Buchta et al., 1973], an autosomal dominant condition with agenesis and/or hypoplasia/dysplasia of the kidney [Squiers et al., 1987; McPherson et al., 1987; Murugasu et al., 1991]. Some investigators have reported the condition as an autosomal recessive trait [Cain et al., 1974; Cole et al., 1976; Pashayan et al., 1977; Schinzel et al., 1978; Monn et al., 1984].

Since nonsyndromal diffuse cystic dysplasia could be an inherited condition, evaluation of fetal kidneys is recommended in families with cystic renal dysplasia. Careful ultrasound examinations of the relatives of individuals with nonsyndromal diffuse cystic renal dysplasia may provide further information in understanding the cause of this rare anomaly.

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